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## SEQUENCE LISTING

<110>	Isis Pharmaceuticals Inc. Rosanne M. Crooke Mark J. Graham	
<120>	MODULATION OF APOLIPOPROTEIN(A) EXPRESSION	
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gca Ala 245	ccg Pro	act Thr	gag Glu	caa Gln	agg Arg 250	cct Pro	GJÀ aàa	gtg Val	cag Gln	gag Glu 255	Cys	tac Tyr	cat His	ggt Gly	aat Asn 260	825
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tgc Cys	caa Gln	gct Ala	tgg Trp 280	tca Ser	tct Ser	atg Met	aca Thr	cca Pro 285	cac His	tcg Ser	cat His	agt Ser	cgg Arg 290	acc Thr	cca Pro	921
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gat Asp	gct Ala 310	Val	gca Ala	gct Ala	cct Pro	tat Tyr 315	tgt Cys	tat Tyr	acg Thr	agg Arg	gat Asp 320	Pro	ggt Gly	gtc Val	agg Arg	1017
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gto Val	gc <u>c</u> Ala	g cct	ceg Pro	act Thr 345	Val	acc Thr	ccg	gtt Val	cca Pro	ser	cta Leu	gag Glu	gct Ala	Pro 355	tcc Ser	1113
gaa Glu	ı caa ı Glr	gca Ala	a ccg a Pro 360	Thr	gag Glu	caa Gln	ago Aro	g cct g Pro 365	GT?	gto Val	g cag Glr	gag Glu	tgo Cys 370	TAI	cat His	1161
ggt Gl <sub>)</sub>	aat Ası	gga 1 Gl	y Glr	g agt 1 Ser	tat Tyr	cga Arg	380 380	Thr	tac Tyi	tco Sei	c acc	act Thr 385	. val	e aca	a gga Gly	1209
aga Arg	a acc g Thi 39	с Су	c caa s Glr	a gct n Ala	tgg Trp	g tca Ser 395	: Sei	atg Met	g aca	e cca	a cad His 400	s Sei	g cat	agt Ser	c cgg	1257
ace Th: 40!	r Pro	a ga o Gl	a tad u Tyi	tac Tyi	c cca c Pro 410	a Ası	gct Ala	t ggo a Gly	c tto y Le	ate 1 Ile 41	e Met	g aad t Asi	tac Tyi	c tgo	agg Arg 420	1305

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gtc Val	agg Arg	tgg Trp	gag Glu 440	tac Tyr	tgc Cys	aac Asn	ctg Leu	acg Thr 445	caa Gln	tgc Cys	tca Ser	gac Asp	gca Ala 450	gaa Glu	glà aaa	1401
act Thr	gcc Ala	gtc Val 455	gcg Ala	cct Pro	ccg Pro	act Thr	gtt Val 460	acc Thr	ccg Pro	gtt Val	cca Pro	agc Ser 465	cta Leu	gag Glu	gct Ala	1449
cct Pro	tcc Ser 470	gaa Glu	caa Gln	gca Ala	ccg Pro	act Thr 475	gag Glu	caa Gln	agg Arg	cct Pro	ggg Gly 480	gtg Val	cag Gln	gag Glu	tgc Cys	1497
tac Tyr 485	cat His	ggt Gly	aat Asn	gga Gly	cag Gln 490	agt Ser	tat Tyr	cga Arg	ggc	aca Thr 495	tac Tyr	tcc Ser	acc Thr	act Thr	gtc Val 500	1545
aca Thr	gga Gly	aga Arg	acc Thr	tgc Cys 505	caa Gln	gct Ala	tgg Trp	tca Ser	tct Ser 510	atg Met	aca Thr	cca Pro	cac His	tcg Ser 515	cat His	1593
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tgc Cys	agg Arg	aat Asn 535	cca Pro	gat Asp	gct Ala	gtg Val	gca Ala 540	gċt Ala	cct Pro	tat Tyr	tgt Cys	tat Tyr 545	acg Thr	agg Arg	gat Asp	1689
ccc Pro	ggt Gly 550	gtc Val	agg Arg	tgg Trp	gag Glu	tac Tyr 555	tgc Cys	aac Asn	ctg Leu	acg Thr	caa Gln 560	tgc Cys	tca Ser	gac Asp	gca Ala	1737
gaa Glu 565	Gly 999	act Thr	gcc Ala	gtc Val	gcg Ala 570	cct Pro	ccg. Pro	act Thr	gtt Val	acc Thr 575	.ccg Pro	gtt Val	cca Pro	agc Ser	cta Leu 580	1785
gag Glu	gct Ala	cct Pro	tcc Ser	gaa Glu 585	caa Gln	gca Ala	ccg Pro	act Thr	gag Glu 590	caa Gln	agg Arg	cct Pro	ggg ggg	gtg Val 595	cag Gln	1833
gag Glu	tgc Cys	tac Tyr	cat His 600	ggt Gly	aat Asn	gga Gly	cag Gln	agt Ser 605	tat Tyr	cga Arg	ggc	aca Thr	tac Tyr 610	tcc Ser	acc Thr	1881
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			tcc Ser							2169
			cat His							2217
			gga Gly 730							2265
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			agg Arg							2361
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			Gly aaa							2457
			gct Ala 810							2505
			tgc Cys							2553
			gtc Val							2601
_		_	cat His	_		_			_	2649
			tac Tyr							2697

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acg Thr	caa Gln	tgc Cys	tca Ser	gac Asp 905	gca Ala	gaa Glu	ggg	act Thr	gcc Ala 910	gtc Val	gcg Ala	cct Pro	ccg Pro	act Thr 915	gtt Val	2793
												gca Ala				2841
												gga Gly 945				2889
cga Arg	ggc Gly 950	aca Thr	tac Tyr	tcc Ser	acc Thr	act Thr 955	gtc Val	aca Thr	gga Gly	aga Arg	acc Thr 960	tgc Cys	caa Gln	gct Ala	tgg Trp	2937
tca Ser 965	tct Ser	atg Met	aca Thr	cca Pro	cac His 970	tcg Ser	cat His	agt Ser	cgg Arg	acc Thr 975	cca Pro	gaa Glu	tac Tyr	tac Tyr	cca Pro 980	2985
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act Thr 1049	Glu	caa Gln	agg Arg	cct Pro	999 Gly 1050	Val	cag Gln	gag Glu	cya Cya	tac Tyr 1059	His	ggt Gly	aat Asn	gga Gly	cag Gln 1060	3225
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gct Ala	tgg Trp	tca Ser	tct Ser 1080	Met	aca Thr	cca Pro	cac His	t <i>c</i> g Ser 1085	His	agt Ser	cgg Arg	acc Thr	cca Pro 1090	Glu	tac Tyr	3321
tac Tyr	cca Pro	aat Asn 1095	Ala	ggc Gly	ttg Leu	atc Ile	atg Met 1100	Asn	tac Tyr	tgc Cys	agg Arg	aat Asn 1105	Pro	gat Asp	gct Ala	3369
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gca ccg act gag Ala Pro Thr Glu 1160	Gln Arg Pro	ggg gtg cag Gly Val Gln 1165	Glu Cys Tyr Hi	at ggt aat 3561 Ls Gly Asn 170
gga cag agt tat Gly Gln Ser Tyr 1175	cga ggc aca Arg Gly Thr	tac tcc acc Tyr Ser Thr 1180	act gtc aca gg Thr Val Thr Gl 1185	ga aga acc 3609 Ly Arg Thr
tgc caa gct tgg Cys Gln Ala Trp 1190	tca tct atg Ser Ser Met 119	Thr Pro His	tcg cat agt cg Ser His Ser An 1200	gg acc cca 3657 gg Thr Pro
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tgg gag tac tgc Trp Glu Tyr Cys 124	Asn Leu Thr	caa tgc tca Gln Cys Ser 1245	Asp Ala Glu G	gg act gcc 3801 ly Thr Ala 250
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cca cac tcg Pro His Ser 165	His Ser Arg 7	acc cca gaa t Thr Pro Glu T 1660	ac tac cca aat Yr Tyr Pro Asn 166	Ala Gly Leu	5049
atc atg aac Ile Met Asn 1670	Tyr Cys Arg A	aat cca gat g Asn Pro Asp A L675	get gtg gea get Ala Val Ala Ala 1680	cct tat tgt Pro Tyr Cys	5097
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atg aca cca Met Thr Pro 1765	cac tcg cat a His Ser His 3 1770	agt cgg acc o Ser Arg Thr E	cca gaa tac tac Pro Glu Tyr Tyr 1775	cca aat gct Pro Asn Ala 1780	5385
ggc ttg atc Gly Leu Ile	atg aac tac Met Asn Tyr ( 1785	Cys Arg Asn E	cca gat gct gtg Pro Asp Ala Val 1790	g gca gct cct . Ala Ala Pro 1795	5433
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cga ggc aca tac Arg Gly Thr Tyr	tcc acc act gr Ser Thr Thr Va 1865	cc aca gga ag al Thr Gly Ai 1870	ga acc tgc caa rg Thr Cys Gln	gct tgg 5673 Ala Trp 1875
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aat gct ggc ttg Asn Ala Gly Leu 1895	Ile Met Asn T	ac tgc agg aa yr Cys Arg An 900	at cca gat gct sn Pro Asp Ala 1905	gtg gca 5769 Val Ala
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act gag caa agg Thr Glu Gln Arg 1960	Pro Gly Val G	ag gag tgc to ln Glu Cys T 1965	ac cat ggt aat yr His Gly Asn 1970	Gly Gln
agt tat cga ggc Ser Tyr Arg Gly 1975	Thr Tyr Ser T	cc act gtc a hr Thr Val T 980	ca gga aga acc hr Gly Arg Thr 1985	tgc caa 6009 Cys Gln
gct tgg tca tct Ala Trp Ser Ser 1990	atg aca cca c Met Thr Pro H 1995	ac tcg cat a is Ser His S	gt cgg acc cca er Arg Thr Pro 2000	gaa tac 6057 Glu Tyr
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gca ccg act gag ca Ala Pro Thr Glu Gl 2070	a agg cct ggg n Arg Pro Gly 2075	gtg cag gag Val Gln Glu	tgc tac cat of Cys Tyr His 0 2080	ggt aat 6297 Gly Asn
gga cag agt tat cg Gly Gln Ser Tyr Ar 2085			Val Thr Gly A	
tgc caa gct tgg tc Cys Gln Ala Trp Se 21			His Ser Arg	
gaa tac tac cca aa Glu Tyr Tyr Pro As 2120				
gat gct gtg gca gc Asp Ala Val Ala Al 2135		Tyr Thr Arg		
tgg gag tac tgc aa Trp Glu Tyr Cys As 2150				
gtc gcg cct ccg ac Val Ala Pro Pro Th 2165			Leu Glu Ala I	
gaa caa gca ccg ac Glu Gln Ala Pro Th 21			Gln Glu Cys 7	
ggt aat gga cag ag Gly Asn Gly Gln Se 2200				
aga acc tgc caa gc Arg Thr Cys Gln Al 2215		Met Thr Pro		
acc cca gaa tac ta Thr Pro Glu Tyr Ty 2230				
aat cca gat gct gt Asn Pro Asp Ala Va 2245		_	Thr Arg Asp I	
gtc agg tgg gag ta Val Arg Trp Glu Ty 22			Ser Asp Ala C	

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act gcc gt Thr Ala Va	c gcg cct l Ala Pro 2280	ccg act Pro Thr	gtt acc Val Thr 228	Pro Val	cca agc Pro Ser	cta gag Leu Glu 2290	gct 69 Ala	21
cct tcc ga Pro Ser Gl 22	a caa gca u Gln Ala 95	ccg act Pro Thr	gag caa Glu Gln 2300	agg cct Arg Pro	ggg gtg Gly Val 230	Gln Glu	tgc 69 Cys	69
tac cat go Tyr His Gl 2310	t aat gga y Asn Gly	cag agt Gln Ser 231	Tyr Arg	ggc aca Gly Thr	tac tcc Tyr Ser 2320	acc act Thr Thr	gtc 70 Val	17
aca gga ag Thr Gly Ar 2325	a acc tgo g Thr Cys	caa gct Gln Ala 2330	tgg tca Trp Ser	tct atg Ser Met 233	Thr Pro	cac tcg His Ser	cat 70 His 2340	65
agt cgg ac Ser Arg Th	c cca gaa ir Pro Glu 234	Tyr Tyr	cca aat Pro Asn	gct ggc Ala Gly 2350	ttg atc Leu Ile	atg aac Met Asn 235	Tyr	13
tgc agg aa Cys Arg As	it cca gat on Pro Asp 2360	gct gtg Ala Val	gca gct Ala Ala 236	Pro Tyr	tgt tat Cys Tyr	acg agg Thr Arg 2370	gat 71 Asp	61
ccc ggt gt Pro Gly Va	c agg tgg ll Arg Tr <u>r</u> 375	g gag tac Glu Tyr	tgc aac Cys Asn 2380	ctg acg Leu Thr	caa tgc Gln Cys 238	Ser Asp	gca 72 Ala	09
gaa ggg ac Glu Gly Th 2390	et gee gto ir Ala Val	gcg cct Ala Pro 239	Pro Thr	gtt acc Val Thr	ccg gtt Pro Val 2400	cca agc Pro Ser	cta 72 Leu	57
gag gct co Glu Ala Pr 2405	ct tcc gaa co Ser Glu	a caa gca n Gln Ala 2410	ccg act Pro Thr	gag caa Glu Gln 241	Arg Pro	ggg gtg Gly Val	cag 73 Gln 2420	05
gag tớc tá Glu Cys Ty	ac cat ggt or His Gly 242	Asn Gly	cag agt Gln Ser	tat cga Tyr Arg 2430	ggë aca Gly Thr	tac tcc Tyr Ser 243	Thr	53
act gtc ac Thr Val Th		_	_	Trp Ser	_			01
tcg cat as Ser His Se 24						Leu Ile		49
aac tac to Asn Tyr Cy 2470			Ala Val					97
agg gat co Arg Asp Pi 2485					Leu Thr			45
gac gca ga Asp Ala Gl	aa ggg act lu Gly Thi	gcc gtc Ala Val	gcg cct Ala Pro	ccg act Pro Thr	gtt acc Val Thr	ccg gtt Pro Val		93

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								-1	.3 -							
				2505	;				2510	)				2515	;	
agc ( Ser ]	cta Leu	gag Glu	gct Ala 2520	Pro	tcc Ser	gaa Glu	caa Gln	gca Ala 2525	Pro	act Thr	gag Glu	caa Gln	agg Arg 2530	Pro	Gly ggg	7641
gtg ( Val (	cag Gln	gag Glu 2535	Сув	tac Tyr	cat His	ggt Gly	aat Asn 2540	Gly	cag Gln	agt Ser	tat Tyr	cga Arg 2545	Gly	aca Thr	tac Tyr	7689
tcc a	acc Thr 2550	Thr	gtc Val	aca Thr	gga Gly	aga Arg 2555	Thr	tgc Cys	caa Gln	gct Ala	tgg Trp 2560	Ser	tct Ser	atg Met	aca Thr	7737
cca ( Pro 1 2565	cac His	tcg Ser	cat His	agt Ser	cgg Arg 2570	Thr	cca Pro	gaa Glu	tac Tyr	tac Tyr 2575	Pro	aat Asn	gct Ala	ggc	ttg Leu 2580	7785
atc a	atg Met	aac Asn	tac Tyr	tgc Cys 2585	Arg	aat Asn	cca Pro	gat Asp	gct Ala 2590	Val	gca Ala	gct Ala	cct Pro	tat Tyr 2595	Cys	7833
tat a	acg Thr	agg Arg	gat Asp 2600	Pro	ggt Gly	gtc Val	agg Arg	tgg Trp 2605	Glu	tac Tyr	tgc Cys	aac Asn	ctg Leu 2610	Thr	caa Gln	7881
tgc Cys	tca Ser	gac Asp 2615	Ala	gaa Glu	gjà aaa	act Thr	gcc Ala 2620	Val	gcg Ala	cct Pro	ccg Pro	act Thr 2625	Val	acc Thr	ccg Pro	7929
gtt Val	cca Pro 2630	Ser	cta Leu	gag Glu	gct Ala	cct Pro 2635	Ser	gaa Glu	caa Gln	gca Ala	ccg Pro 2640	Thr	gag Glu	cag Gln	agg Arg	7977
cct Pro 2645	Gly	gtg Val	cag Gln	gag Glu	tgc Cys 2650	Tyr	cac His	ggt Gly	Asn	gga Gly 2655	Gln	agt Ser	tat Tyr	cga Arg	ggc Gly 2660	8025
aca Thr	tac Tyr	tcc Ser	acc Thr	act Thr 266	Val	act Thr	gga Gly	aga Arg	acc Thr 267	Cys	caa Gln	gct Ala	tgg Trp	tca Ser 267	Ser	8073
atg Met				Ser					Pro					Asn		8121
ggc Gly	ttg Leu	atc Ile 269	Met	aac Asn	tac Tyr	tgc Cys	agg Arg 2700	Asn	cca Pro	gat Asp	gct Ala	gtg Val 270!	Ala	gct Ala	cct Pro	8169
tat Tyr		Tyr					Gly					Tyr				8217
acg Thr 2725	Gln	tgc Cys	tca Ser	gac Asp	gca Ala 2730	Glu	gjå aaa	act Thr	gcc Ala	gtc Val 2735	Ala	cct Pro	ccg Pro	act Thr	gtt Val 2740	8265

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acc Thr	ccg Pro	gtt Val	cca Pro	agc Ser 2745	Leu	gag Glu	gct Ala	cct Pro	tcc Ser 2750	Glu	caa Gln	gca Ala	ccg Pro	act Thr 2755	Glu	8313
caa Gln	agg Arg	cct Pro	999 Gly 2760	Val	cag Gln	gag Glu	tgc Cys	tac Tyr 2765	His	ggt Gly	aat Asn	gga Gly	cag Gln 2770	Ser	tat Tyr	8361
cga Arg	ggc Gly	aca Thr 2775	Tyr	tcc Ser	acc Thr	act Thr	gtc Val 2780	Thr	gga Gly	aga Arg	acc Thr	tgc Cys 2785	caa Gln	gct Ala	tgg Trp	8409
tca Ser	tct Ser 2790	Met	aca Thr	cca Pro	cac His	tcg Ser 279	His	agt Ser	cgg Arg	acc Thr	cca Pro 2800	Glu	tac Tyr	tac Tyr	cca Pro	8457
aat Asn 2805	Ala	ggc Gly	ttg Leu	atc Ile	atg Met 281(	Asn	tac Tyr	tgc Cys	agg Arg	aat Asn 281	Pro	gat Asp	gct Ala	gtg Val	gca Ala 2820	8505
gct Ala	cct Pro	tat Tyr	tgt Cys	tat Tyr 282	Thr	agg Arg	gat Asp	ccc Pro	ggt Gly 2830	Val	agg Arg	tgg Trp	gag Glu	tac Tyr 2835	Сув	8553
aac Asn	ctg Leu	acg Thr	caa Gln 284	Cys	tca Ser	gac Asp	gca Ala	gaa Glu 284!	Gly	act Thr	gcc Ala	gtc Val	gcg Ala 2850	Pro	ccg Pro	8601
act Thr	gtt Val	acc Thr 285	Pro	gtt Val	cca Pro	agc Ser	cta Leu 286	Glu	gct Ala	cct Pro	tcc Ser	gaa Glu 286!	caa Gln 5	gca Ala	ccg Pro	8649
act Thr	gag Glu 287	Gln	agg Arg	cct Pro	Gly aaa	gtg Val 287	Gln	gag Glu	tgc Cys	tac Tyr	cat His 288	Gly	aat Asn	gga Gly	cag Gln	8697
agt Ser 288	Tyr	cga Arg	ggc	aca Thr	tac Tyr 289	Ser	acc Thr	act Thr	gtc Val	aca Thr 289	Gly	aga Arg	acc Thr	tgc Cys	caa Gln 2900	8745
gct Ala	tgg Trp	tca Ser	tct Ser	atg Met 290	Thr	cca Pro	cac His	tcg Ser	cat His 291	Ser	cgg Arg	acc Thr	cca Pro	gaa Glu 291	Tyr	8793
tac Tyr	cca Pro	aat Asn	gct Ala 292	Gly	ttg Leu	atc Ile	atg Met	aac Asn 292	Tyr	tgc Cys	agg Arg	aat Asn	cca Pro 293	Asp	gct Ala	8841
gtg Val	gca Ala	gct Ala 293	Pro	tat Tyr	tgt Cys	tat Tyr	acg Thr 294	Arg	gat Asp	ccc Pro	ggt Gly	gtc Val 294	agg Arg 5	tgg Trp	gag Glu	8889
tac Tyr	tgc Cys 295	Asn	ctg Leu	acg Thr	caa Gln	tgc Cys 295	Ser	gac Asp	gca Ala	gaa Glu	999 Gly 296	Thr	gcc Ala	gtc Val	gcg Ala	8937
cct Pro	ccg Pro	act Thr	gtt Val	acc Thr	ccg Pro	gtt Val	cca Pro	agc Ser	cta Leu	gag Glu	gct Ala	cct Pro	tcc Ser	gaa Glu	caa Gln	8985

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2965	2970	2975	2980
gca ccg act gag cag Ala Pro Thr Glu Gln 298	agg cct ggg gtg cag Arg Pro Gly Val Gln 5 2990	Glu Cys Tyr His Gly	Asn
gga cag agt tat cga Gly Gln Ser Tyr Arg 3000	ggc aca tac tcc acc Gly Thr Tyr Ser Thr 3005	act gtc act gga aga Thr Val Thr Gly Arg 3010	acc 9081 Thr
tgc caa gct tgg tca Cys Gln Ala Trp Ser 3015	tct atg aca cca cac Ser Met Thr Pro His 3020	tcg cat agt cgg acc Ser His Ser Arg Thr 3025	cca 9129 Pro
gaa tac tac cca aat Glu Tyr Tyr Pro Asn 3030	gct ggc ttg atc atg Ala Gly Leu Ile Met 3035	aac tac tgc agg aat Asn Tyr Cys Arg Asn 3040	cca 9177 Pro
gat gct gtg gca gct Asp Ala Val Ala Ala 3045	cct tat tgt tat acg Pro Tyr Cys Tyr Thr 3050	agg gat ccc ggt gtc Arg Asp Pro Gly Val 3055	agg 9225 Arg 3060
tgg gag tac tgc aac Trp Glu Tyr Cys Asn 306	ctg acg caa tgc tca Leu Thr Gln Cys Ser 5 3070	Asp Ala Glu Gly Thr	Ala
gtc gcg cct ccg act Val Ala Pro Pro Thr 3080	gtt acc ccg gtt cca Val Thr Pro Val Pro 3085	agc cta gag gct cct Ser Leu Glu Ala Pro 3090	tcc 9321 Ser
	gag cag agg cct ggg Glu Gln Arg Pro Gly 3100		
ggt aat gga cag agt Gly Asn Gly Gln Ser 3110	tat cga ggc aca tac Tyr Arg Gly Thr Tyr 3115	tcc acc act gtc act Ser Thr Thr Val Thr	gga 9417 Gly
	tgg tca tct atg aca Trp Ser Ser Met Thr 3130		
acc cca gaa tac tac Thr Pro Glu Tyr Tyr 314	cca aat gct ggc ttg Pro Asn Ala Gly Leu 5 3150	Ile Met Asn Tyr Cys	Arg
aat cca gat gct gtg Asn Pro Asp Ala Val 3160	gca gct cct tat tgt Ala Ala Pro Tyr Cys 3165	tat acg agg gat ccc Tyr Thr Arg Asp Pro 3170	ggt 9561 Gly
gtc agg tgg gag tac Val Arg Trp Glu Tyr 3175	tgc aac ctg acg caa Cys Asn Leu Thr Gln 3180	tgc tca gac gca gaa Cys Ser Asp Ala Glu 3185	ggg 9609
	ccg act gtt acc ccg Pro Thr Val Thr Pro 3195		

cct tcc gaa Pro Ser Glu 3205	Gln Ala F	ecg act gag Pro Thr Glu 3210	g cag agg ı Gln Arg	cct ggg Pro Gly 3215	gtg cag Val Gln	gag tgc Glu Cys 3220	9705
tac cac ggt Tyr His Gly	aat gga o Asn Gly G 3225	cag agt ta Sln Ser Ty	cga ggc r Arg Gly 323	Thr Tyr	tcc acc Ser Thr	act gtc Thr Val 3235	9753
act gga aga Thr Gly Arg	acc tgc o Thr Cys 0 3240	caa gct tg Gln Ala Tr	g tca tct p Ser Ser 3245	atg aca Met Thr	cca cac Pro His 3250	Ser His	9801
agt cgg acc Ser Arg Thr 325	Pro Glu I	tac tac cc Fyr Tyr Pro 32	o Asn Ala	Gly Leu	atc atg Ile Met 3265	aac tac Asn Tyr	9849
tgc agg aat Cys Arg Asn 3270	cca gat o Pro Asp P	gct gtg gc Ala Val Al 3275	a gct cct a Ala Pro	tat tgt Tyr Cys 3280	Tyr Thr	agg gat Arg Asp	9897
ccc ggt gtc Pro Gly Val 3285	Arg Trp (	gag tac tg Glu Tyr Cy 3290	c aac ctg s Asn Lev	acg caa Thr Gln 3295	tgc tca Cys Ser	gac gca Asp Ala 3300	9945
gaa ggg act Glu Gly Thr	gee gte g Ala Val A 3305	geg eet ee Ala Pro Pr	g act gtt o Thr Val 331	Thr Pro	gtt cca Val Pro	agc cta Ser Leu 3315	9993
gag gct cct Glu Ala Pro	tcc gaa o Ser Glu ( 3320	caa gca cc Gln Ala Pr	g act gag o Thr Glu 3325	g cag agg Gln Arg	cct ggg Pro Gly 333	Val Gln	10041
gag tgc tac Glu Cys Tyr 333	His Gly	aat gga ca Asn Gly Gl 33	n Ser Tyr	cga ggc Arg Gly	aca tac Thr Tyr 3345	tcc acc Ser Thr	10089
act gtc act Thr Val Thr 3350	ggaraga a Gly Arg	acc tgc ca Thr Cys Gl 3355	a get tge n Ala Tr	Ser Ser 3360	Met Thr	cca cac Pro His	10137
tcg cat agt Ser His Ser 3365	Arg Thr	cca gaa ta Pro Glu Ty 3370	c tac cca r Tyr Pro	a aat gct Asn Ala 3375	ggc ttg Gly Leu	atc atg Ile Met 3380	10185
aac tac tgo Asn Tyr Cys	agg aat o Arg Asn 1 3385	Pro Asp Pr	t gtg gca o Val Ala 339	a Ala Pro	tat tgt Tyr Cys	tat acg Tyr Thr 3395	10233
agg gat ccc Arg Asp Pro	e agt gtc a Ser Val 3 3400	agg tgg ga Arg Trp Gl	g tac tgo u Tyr Cyr 3405	aac ctg Asn Leu	aca caa Thr Gln 341	Cys Ser	10281
gac gca gaa Asp Ala Glu 341	Gly Thr	Ala Val Al	g cct cca a Pro Pro 20	a act att o Thr Ile	acc ccg Thr Pro 3425	att cca Ile Pro	10329
agc cta gag Ser Leu Glu	g gct cct	tct gaa ca Ser Glu Gl	a gca cca n Ala Pro	a act gag o Thr Glu	caa agg Gln Arg	cct ggg Pro Gly	10377

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3430	3435	3440	
Val Gln Glu Cys Tyr H	ac gga aat gga cag agt dis Gly Asn Gly Gln Ser 450 345	Tyr Gln Gly Thr Tyr	5
ttc att act gtc aca g	ga aga acc tgc caa gct	tgg tca tct atg aca 10473	3
Phe Ile Thr Val Thr G	ly Arg Thr Cys Gln Ala	a Trp Ser Ser Met Thr	
3465	3470	3475	
cca cac tcg cat agt c	gg acc cca gca tac tac	c cca aat gct ggc ttg 10521	1
Pro His Ser His Ser A	rg Thr Pro Ala Tyr Tyr	c Pro Asn Ala Gly Leu	
3480	3485	3490	
atc aag aac tac tgc c	ga aat cca gat cct gtg	g gca gcc cct tgg tgt 10569	9
Ile Lys Asn Tyr Cys A	rg Asn Pro Asp Pro Val	L Ala Ala Pro Trp Cys	
3495	3500	3505	
tat aca aca gat ccc a	gt gtc agg tgg gag tac	c tgc aac ctg aca cga 10617	7
Tyr Thr Thr Asp Pro S	er Val Arg Trp Glu Tyr	c Cys Asn Leu Thr Arg	
3510	3515	3520	
Cys Ser Asp Ala Glu T	gg act gcc ttc gtc cct rp Thr Ala Phe Val Pro 5330 353	Pro Asn Val Ile Leu	5
gct cca agc cta gag g	oct ttt ttt gaa caa gca	a ctg act gag gaa acc 10713	3
Ala Pro Ser Leu Glu A	la Phe Phe Glu Gln Ala	a Leu Thr Glu Glu Thr	
3545	3550	3555	
ccc ggg gta cag gac t	gc tac tac cat tat gga	a cag agt tac cga ggc 10761	1
Pro Gly Val Gln Asp C	ys Tyr Tyr His Tyr Gly	y Gln Ser Tyr Arg Gly	
3560	3565	3570	
	gtc aca gga aga act tgc Val Thr Gly Arg Thr Cys 3580		9
	eat agt cgg acc cca gaa His Ser Arg Thr Pro Glu 3595		7
Gly Leu Thr Arg Asn T	ac tgc agg aat cca gat Tyr Cys Arg Asn Pro Asy 1610 361	o Ala Glu Ile Arg Pro	5
	gat ccc agt gtc agg tgg Asp Pro Ser Val Arg Trp 3630		3
aca caa tgc ctg gtg a	ica gaa tca agt gtc ctt	t gca act ctc acg gtg 11001	1
Thr Gln Cys Leu Val T	Thr Glu Ser Ser Val Lei	u Ala Thr Leu Thr Val	
3640	3645	3650	
gtc cca gat cca agc a	aca gag gct tct tct gaa	a gaa gca cca acg gag 11049	9
Val Pro Asp Pro Ser T	Thr Glu Ala Ser Ser Glu	u Glu Ala Pro Thr Glu	
3655	3660	3665	

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caa ag Gln Se 36	ge eed er Pro 570	gly ggg	gtc Val	cag Gln	gat Asp 3675	Cys	tac Tyr	cat His	ggt Gly	gat Asp 3680	Gly	cag Gln	agt Ser	tat Tyr	11097
cga gg Arg Gl 3685	gc tca Ly Sei	ttc Phe	tct Ser	acc Thr 3690	Thr	gtc Val	aca Thr	gga Gly	agg Arg 3695	Thr	tgt Cys	cag Gln	tct Ser	tgg Trp 3700	11145
tcc to Ser Se	ct ato er Met	g aca Thr	cca Pro 3705	His	tgg Trp	cat His	cag Gln	agg Arg 3710	Thr	aca Thr	gaa Glu	tat Tyr	tat Tyr 3715	Pro	11193
aat gg Asn Gl	gt ggo ly Gly	ctg Leu 372	Thr	agg Arg	aac Asn	tac Tyr	tgc Cys 3725	Arg	aat Asn	cca Pro	gat Asp	gct Ala 3730	Glu	att Ile	11241
agt co Ser Pi	ct tgg ro Tri 373	Cys	tat Tyr	acc Thr	atg Met	gat Asp 3740	Pro	aat Asn	gtc Val	aga Arg	tgg Trp 3745	Glu	tac Tyr	tgc Cys	11289
aac ct Asn Le	tg aca eu Thi 750	a caa c Gln	tgt Cys	cca Pro	gtg Val 3755	Thr	gaa Glu	tca Ser	agt Ser	gtc Val 3760	Leu	gcg Ala	acg Thr	tcc Ser	11337
acg go Thr Al	ct gti la Vai	tct L Ser	gaa Glu	caa Gln 3770	Ala	cca Pro	acg Thr	gag Glu	caa Gln 377	Ser	ccc Pro	aca Thr	gtc Val	cag Gln 3780	11385
gac to	gc ta ys Ty:	c cat r His	ggt Gly 378!	Asp	gga Gly	cag Gln	agt Ser	tat Tyr 3790	Arg	ggc Gly	tca Ser	ttc Phe	tcc Ser 379	Thr	11433
act gi			Arg					Trp					Pro		11481
tgg ca		n Arg					Tyr					Leu			11529
aac ta Asn T	ac tg yr Cy 830	c agg s Arg	aat Asn	cca Pro	gat Asp 383	Ala	gag Glu	att Ile	cgc Arg	cct Pro 384	Trp	tgt Cys	tat Tyr	acc Thr	11577
atg g	at 66				+~~	gag	tan	tac	220	ata		<b>C22</b>	tat	cca	11625
Met A 3845	sp Pr	c agt o Ser	Val	Arg 385	$\mathtt{Trp}$	Glu	Tyr	Cys	Asn 385	Leu	Thr	Gln	Cys	Pro 3860	
	sp Pro	o Ser a tca	Val act	Arg 385 ctc Leu	Trp 0 ctc	Glu	Tyr	ccc	Asn 3859 acg Thr	Leu 5 gtg	Thr	Gln	Cys	Pro 3860 cca Pro	11673
3845 gtg a	sp Protest specification to the specification of th	o Ser a tca u Ser g ctt	act Thr 386	Arg 385 ctc Leu 5	Trp 0 ctc Leu gaa	Glu aca Thr	Tyr act Thr	Cys ccc Pro 3870 cca Pro	Asn 3859 acg Thr	Leu 5 gtg Val gaa	Thr gtc Val	cca Pro	gtt Val 3879 act	Pro 3860 cca Pro 5	11673 11721

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3895		3900	3905	
tcc acc act a Ser Thr Thr I 3910	tc aca gga aga le Thr Gly Arg 3915	Thr Cys Gln Ser	tgg tcg tct atg a Trp Ser Ser Met 1 3920	aca 11817 Thr
cca cat tgg c Pro His Trp H 3925	at cgg agg atc is Arg Arg Ile 3930	cca tta tac tat Pro Leu Tyr Tyr 393	c cca aat gct ggc o r Pro Asn Ala Gly : 35	ctg 11865 Leu 3940
acc agg aac t Thr Arg Asn T	ac tgc agg aat Yr Cys Arg Asn 3945	cca gat gct gag Pro Asp Ala Glu 3950	g att cgc cct tgg u Ile Arg Pro Trp 3955	tgt 11913 Cys
Tyr Thr Met A	gat ccc agt gtc Asp Pro Ser Val 1960	agg tgg gag tad Arg Trp Glu Ty 3965	c tgc aac ctg aca r Cys Asn Leu Thr 3970	cga 11961 Arg
tgt cca gtg a Cys Pro Val T 3975	ica gaa tcg agt Thr Glu Ser Ser	gtc ctc aca act Val Leu Thr Th 3980	t ccc aca gtg gcc r Pro Thr Val Ala 3985	ccg 12009 Pro
gtt cca agc a Val Pro Ser 1 3990	aca gag gct cct Thr Glu Ala Pro 3999	Ser Glu Gln Ala	a cca cct gag aaa a Pro Pro Glu Lys 4000	agc 12057 Ser
cct gtg gtc o Pro Val Val 0 4005	cag gat tgc tac Gln Asp Cys Tyr 4010	cat ggt gat gg His Gly Asp Gl 40	a cgg agt tat cga y Arg Ser Tyr Arg 15	ggc 12105 Gly 4020
ata tcc tcc a	acc act gtc aca Thr Thr Val Thr 4025	gga agg acc tg Gly Arg Thr Cy 4030	t caa tct tgg tca s Gln Ser Trp Ser 4035	Ser
Met Ile Pro H	cac tgg cat cag His Trp His Gln 4040	agg acc cca ga Arg Thr Pro Gl 4045	a aac tac cca aat u Asn Tyr Pro Asn 4050	gct 12201 Ala
ggc ctg acc of Gly Leu Thr (	gag aac tac tgc Glu Asn Tyr Cys	agg aat cca ga Arg Asn Pro As 4060	t tct ggg aaa caa p Ser Gly Lys Gln 4065	ccc 12249 Pro
tgg tgt tac a Trp Cys Tyr 3 4070	aca acc gat ccg Thr Thr Asp Pro 407	Cys Val Arg Tr	g gag tac tgc aat p Glu Tyr Cys Asn 4080	ctg 12297 Leu
aca caa tgc 1 Thr Gln Cys 1 4085	tca gaa aca gaa Ser Glu Thr Glu 4090	Ser Gly Val Le	a gag act ccc act au Glu Thr Pro Thr 195	gtt 12345 Val 4100
gtt cca gtt ( Val Pro Val	cca agc atg gag Pro Ser Met Glu 4105	gct cat tct ga Ala His Ser Gl 4110	a gca gca cca act u Ala Ala Pro Thr .4115	Glu
Gln Thr Pro	gtg gtc cgg cag Val Val Arg Gln 4120	tgc tac cat gg Cys Tyr His Gl 4125	gt aat ggc cag agt Ly Asn Gly Gln Ser 4130	tat 12441 Tyr

cga Arg	ggc Gly	aca Thr 4135	Phe	tcc Ser	acc Thr	act Thr	gtc Val 4140	Thr	gga Gly	agg Arg	aca Thr	tgt Cys 4145	Gln	tct Ser	tgg Trp	12489
tca Ser	tcc Ser 4150	Met	aca Thr	cca Pro	cac His	cgg Arg 4155	His	cag Gln	agg Arg	acc Thr	cca Pro 4160	Glu	aac Asn	tac Tyr	cca Pro	12537
aat Asn 4165	gat Asp	ggc Gly	ctg Leu	aca Thr	atg Met 4170	Asn	tac Tyr	tgc Cys	agg Arg	aat Asn 4175	Pro	gat Asp	gcc Ala	gat Asp	aca Thr 4180	12585
ggc Gly	cct Pro	tgg Trp	tgt Cys	ttt Phe 4185	Thr	atg Met	gac Asp	ccc Pro	agc Ser 4190	Ile	agg Arg	tgg Trp	gag Glu	tac Tyr 4195	Cys	12633
aac Asn	ctg Leu	acg Thr	cga Arg 4200	Cys	tca Ser	gac Asp	aca Thr	gaa Glu 4205	Gly	act Thr	gtg Val	gtc Val	gct Ala 421	Pro	ccg Pro	12681
act Thr	gtc Val	atc Ile 4215	Gln	gtt Val	cca Pro	agc Ser	cta Leu 4220	Gly	cct Pro	cct Pro	tct Ser	gaa Glu 4225	Gln	gac Asp	tgt Cys	12729
atg Met	ttt Phe 4230	Gly	aat Asn	Gly 999	aaa Lys	gga Gly 423!	Tyr	cgg Arg	ggc Gly	aag Lys	aag Lys 424(	Ala	acc Thr	act Thr	gtt Val	12777
act Thr 424	ggg ggg 5	acg Thr	cca Pro	tgc Cys	cag Gln 425	Glu	tgg Trp	gct Ala	gcc Ala	cag Gln 425	Glu	ccc Pro	cat His	aga Arg	cac His 4260	12825
agc Ser	acg Thr	ttc Phe	att Ile	cca Pro 426	Gly	aca Thr	aat Asn	aaa Lys	tgg Trp 427	Ala	ggt Gly	ctg Leu	gaa Glu	aaa Lys 427	Asn	12873
tac Tyr	tgc Cys	.cgt Arg	aac Asn 428	Pro	gat Asp	ggt Gly	gac Asp	atc Ile	aat	ggt	-ccc	taa	tgc	tac	aca	12921
			420	U				428		Gly	Pro	Trp	Cys 429	Tyr	Thr	
Met	aat Asn	cca Pro 429	aga Arg	aaa	ctt Leu	ttt Phe	gac	tac Tyr	5 tgt	gat	Pro	Trp	Cys 429 ctc Leu	Tyr 0 tgt	Thr	12969
Met	Asn	Pro 429 tca Ser	aga Arg 5	aaa Lys gat	Leu tgt	Phe	gac Asp 430 aag Lys	428! tac Tyr 0	tgt Cys caa	gat Asp gtg	Pro atc Ile	cct Pro 430 ccg Pro	Cys 429 ctc Leu 5	Tyr 0 tgt Cys aaa	gca Ala tgt	12969
Met tcc Ser	tct Ser 431 gga Gly	Pro 429 tca Ser 0	aga Arg 5 ttt Phe	aaa Lys gat Asp	tgt Cys	ggg Gly 431 ggg Gly	gac Asp 430 aag Lys 5	tac Tyr 0 cct Pro	tgt Cys caa Gln gcc	gat Asp gtg Val	ero atc Ile gag Glu 432 cca Pro	cct Pro 430 ccg Pro	Cys 429 ctc Leu 5 aag Lys	Tyr 0 tgt Cys aaa Lys	gca Ala tgt Cys	
Met tcc Ser cct Pro 432	tct Ser 431 gga Gly	Pro 429 tca Ser 0 agc Ser	aga Arg  ttt Phe att Ile	aaa Lys gat Asp gta Val	tgt Cys ggg Gly 433 aga Arg	ggg Gly 431 ggg Gly 0	gac Asp 430 aag Lys 5 tgt Cys	tac Tyr 0 cct Pro gtg Val	tgt Cys caa Gln gcc Ala	gat Asp gtg Val cac His 433	Pro atc Ile gag Glu 432 cca Pro 5	CCT Pro 430 CCG Pro C Cat His	Cys 429 ctc Leu 5 aag Lys tcc Ser	Tyr 0 tgt Cys aaa Lys tgg Trp	gca Ala tgt Cys ccc Pro 4340 ggc Gly	13017

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	4360		4365		4370	
aag tcc tca Lys Ser Ser 437	Arg Pro Ser	tcc tac Ser Tyr 4380	Lys Val	atc ctg ggt Ile Leu Gly 438!	gca cac caa Ala His Gln 5	13209
gaa gtg aac Glu Val Asn 4390	ctc gaa tct Leu Glu Ser	cat gtt His Val 4395	cag gaa Gln Glu	ata gaa gtg Ile Glu Val 4400	tct agg ctg Ser Arg Leu	13257
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